REMARKS

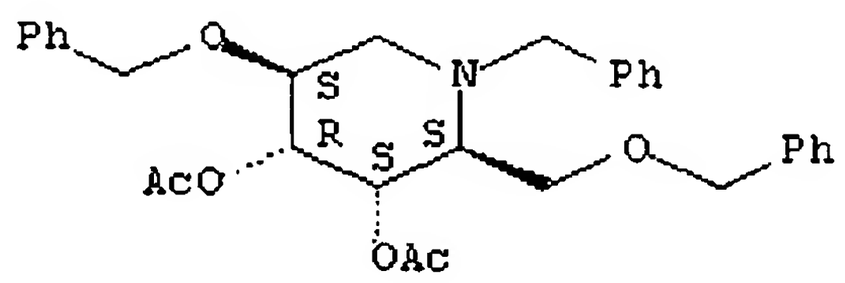
Claims 1, 3, 4 and 20-35 are pending in the current application. Claims 2 and 5-19 were previously cancelled. Claims 4 and 21-35 are withdrawn. Claims 1, 3 and 20 have been rejected. For editorial purposes, claim 1 has been amended to read "in free or pharmaceutically acceptable salt form". Claim 1 has also been amended to delete the term "prodrug'. It is believed no new matter has been added.

Claim Rejections under 35 U.S.C. § 112

Claims 1, 3 and 20 have been rejected under §112, first paragraph for purportedly failure to enable the prodrugs of the invention. Without agreeing as to the accuracy of the Examiner's statements or arguments, Applicants have amended claim 1 to remove the offending language and to expedite allowance of the claims. Withdrawal of the rejections under 35 U.S.C. § 112, first paragraph is respectfully requested.

Claim Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 1, 3 and 20 under 35 U.S.C. § 103(a) as being allegedly obvious in view of WO 02/055498 (hereinafter "WO '498"). In particular, the Examiner identified the compound with the following structure:



which corresponds with the compound listed on lines 21-22 on page 7 of WO '498 as the closest compound. The Examiner argued that the only differences between the claimed compounds and the compound in WO '498 are that (1) the phenyl group on the N1-position of the piperidine ring of the claimed compound is a 4-alkoxy-substituted benzyl group while the benzyl group of the compound of WO '498 is unsubstituted; and that (2) the hydroxy groups on the piperidine ring are protected while the claimed compounds are unprotected, i.e., free hydroxy groups. The Examiner argued that claim 1 of the WO '498 reference teaches that the 4-position of the phenyl group may be substituted with C_{1-6}alkoxy and that that the compound of WO '498, when absent

the protecting group, is the free hydroxy. As such, the Examiner concluded that the claims are obvious.

Applicants respectfully disagree. It is well established that a disclosure of a generic formula does not by itself render obvious a species of that genus. *See In re Baird*, 16 F.3d 380, 382 (Fed. Cir. Jan. 19, 1994) ('The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.")(citing *In re Jones*, 958 F.2d 347, 350 (Fed. Cir. 1992); *See also* MPEP 2144.08. In addition, "[a] disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds.". *In re Baird*, 16 F.3d at 383. To begin a proper obviousness analysis of structurally similar chemical compounds, the Examiner must first identify the lead compound in the prior art. *See Eisai Co. LTD v. Dr. Reddy's Laboratories, LTD.*, 533 F.3d 1353, 1359 (Fed. Cir. July 21, 2008)("a prima facie case of obviousness for a chemical compound [ ] begins with the reasoned identification of a lead compound."). Once identified, the Examiner must also provide adequate support in the art for the change of the lead compound to the claimed invention. *See Takeda Chemical Industries, LTD v. Alpharm PTY., LTD*, 492 F.3d 1350, 1356 (Fed. Cir. June 28, 2007)("[i]n addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of 'adequate support in the prior art' for the change in structure.").

Here, WO '498 generically discloses 2-hydroxymethyl-3,4,5-trihydroxypiperidine compounds having a (2S,4R,5S) configuration useful as GCS inhibitors, wherein the configuration at the 3-position may be (S) or (R). Applicants admit that the claimed compound of Formula I fall within the generic disclosure of WO '498. However, nothing in WO '498 suggests that, of all the possible substituents, the 4-(pentyloxy)-phenyl)methyl substituent at the 1-position of the piperidine or that the (2S,3S,4R,5S) configuration would be preferred, rendering the selection of the claimed compound of Formula I or Formula III obvious. Quite contrary to the Examiner's analysis, one skilled in the art would not have identified the compound having the (2S,3S,4R,5S) configuration and the unsubstituted benzyl substituent at the 1-position as disclosed on page 7 of WO '498 as the lead compound because this reference specifically excludes such compound from their invention. *See* WO 02/055498, page 7, lines 15-22 ("there is provided a compound of formula (III) [ ], provided that the compound is not: piperidine, 1-phenylmethyl-3,4,5-di(acetyloxy)-5-(phenylmethoxy)-2-[(phenylmethoxy)-

methyl], (2S,3S,4R,5S);") (*emphasis added*). In fact, WO '498 explicitly teaches away from selecting the (2S,3S,4R,5S) compounds of Formula I and Formula III of the current invention as WO '498 explicitly discloses that the (3R) configuration is preferred. *See* WO 02/055498 page 4, lines 12-13. In looking at WO '498, particularly Table 2 on page 27, one skilled in the art may identify compounds of Examples 2 and 3, which have the (2S,3R,4R,5S) configuration, as the lead compounds since those two compounds have good IC_{50} and selectivities against human GCS. In addition, the data with respect to glucosyl ceramide synthase (hereafter GCS) inhibition for the compound of example 5 of WO '498, which has the (2S,3S,4R,5S) configuration, are not so good compared to the reference compound NB-DGJ and the compound of example 2. See WO 02/055498, page 27, Table 1. The only difference between the compound of example 5 the compound of example 2 is that the hydroxy group at position 3 has either the absolute (*R*)-configuration (in the case of the compound of example 2) or the absolute (*S*)-configuration (in the case of the compound of example 5). Therefore, one skilled in the art who knew of WO '498 and sought new GCS inhibitors, would certainly not have made further compounds of WO '498 wherein the hydroxy group at position 3 has the absolute (*S*)-configuration, because he would have thought that compounds with the absolute (*S*)-configuration would not give interesting results. Consequently, finding that the compounds of the current invention had interesting GCS inhibition properties was certainly novel and unobvious at the filing date of the instant patent application. In view of the arguments, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a).

Claim Rejections for Double Patenting

The Examiner provisionally rejected claims 1, 3 and 20 as being unpatentable over claims 1-10 and 13 of copending application number 10/522,207 (the '207 application) on the ground of nonstatutory obviousness type double patenting for the compounds of the two cases are allegedly not patentably distinct.

Applicants respectfully disagree. The '207 application, although claims (2S,3S,4R,5S) 2-hydroxymethyl-3,4,5-trihydroxypiperidine compounds having a substituted benzyl substituent at the 1-position of the piperidine, the benzyl substituent is allowed to be substituted with very many different substituents, but a pentyloxy group. As discussed above, "a prima facie case of obviousness for a chemical compound [ ] begins with the reasoned identification of a lead

compound." *Eisai*, 533 F.3d at 1359. In addition to the lead compound, the art must also provide some kind of suggestion for the change in the structure to arrive at the claimed invention. Here, nothing in the ''207 application suggests that pentyloxy is desirable. It is respectfully submitted that the Examiner has not met her burden of showing prima facie obviousness to support the nonstatutory obviousness type double patenting rejection. Reconsideration and withdrawal of this rejection is earnestly and respectfully requested.

This response is filed within three months from the date of the mailing of the non-final office action dated April 6, 2010, which response is due July 6, 2010, it is believed this response is timely and no fees are required. If this is not correct, however, please charge any additional fees, or credit any overpayment, to Deposit Account No. 50-4255

Respectfully submitted,

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